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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,980	04/24/2006	Edwin Andries Gerard Van Der Vossen	13477-00002-US	4140

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EXAMINER	
ZHENG, LI	

ART UNIT	PAPER NUMBER
1638	

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10/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,980	VAN DER VOSSEN ET AL.	
	Examiner	Art Unit	
	LI ZHENG	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,39 and 44-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,39 and 44-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 8, 2008 has been entered.

2. Applicant's cancellation of claim 8-32, 34-38 and 40-43, amendments to claim 1, as well as submission of new claims 47-48 filed on 7/8/2008 are acknowledged.

As a result, claims 1, 3-7, 39 and 44-48 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The objections and rejections not set forth in this action are withdrawn.

Claim Rejections - 35 USC § 112

5. Claims 1, 3-7, 39 and 44-46 remain rejected and claims 47-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record stated in the Office action mailed January 8, 2008. Applicants traverse in the paper July 8, 2008. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that since the possession of an invention can be shown by description of an actual reduction to practice, the present application describes an actual reduction to practice of the claimed method in Example 12 (response, page 6, 2nd paragraph).

The Office contends that Example 12 demonstrate that complementation analysis is used to clone and to verify the genomic DNA encoding Rpi-blb2 gene. However, the instant claims are not so limited to the nucleic acid molecule encoding the polypeptide depicted in SEQ ID NO: 2 and 4 or the nucleic acid molecule of SEQ ID NO: 3,5 or 6.

Applicants further argue that claim 1 is amended so that it requires a higher level of identity than that of Example 11A of the new Written Description Guidelines (response, the paragraph bridging pages 6-7 and page 7, 2nd paragraph).

The Office contends that Example 11A of the new Written Description Guidelines indicates that when there is no functional limitation on the nucleic acid (e.g. claim 1 in Example 11A), the written description requirement for the claimed genus is met. However, when there is a functional limitation on the nucleic acid (e.g. claim 2 in Example 11A), the written description requirement is not met. In the instant claims, the claimed genus of Rpi-blb2 protein encoding nucleotide sequences have a functional limitation, which is increase the resistance of a plant to a plant pathogen of the phylum Oomyceta. There is no disclosed correlation between structure and function and there is no known disclosed protein having antifungal activity except for SEQ ID NO: 2 or 4. While general knowledge in the art may have allowed one of skill in the art to identify other proteins expected to have the same or similar tertiary structure, in this case there is no general knowledge in the art about antifungal activity to suggest that general similarity of structure confers the activity. Accordingly, a person skilled in the art would not accept the disclosure of SEQ ID NO: 2 or 4 as representative of other proteins having antifungal activity.

Applicants further present the board's decision on *Ex parte Sun* to support that a genus of polynucleotides having 80% identity to the coding region of the sequence is described and enabled (response, page 7, 2nd paragraph).

The Office contends that the instant case has different factual basis compared to *Ex parte Sun* . For the WEE1 protein, it was known in the art that the variations in amino acid sequences of WEE1 are in the amino terminus while the carboxyl end of the genes are relative conserved. It was also known that the carboxyl terminus and central portion

of the WEE1 protein from S. pombe contain the protein kinase domains and sequence crucial for substrate recognition and catalysis (page 10).

Applicants further argue that the basis for written description rejection towards the hybridization language is unclear (response, page 7, 4th paragraph).

The Office contends that the reasoning for the rejection is discussed in previous office action filed January 8, 2008. The state-of-the-art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40:857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^{0}C (page 859, left column, 2nd paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotides mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment of Frourgoux-Nicol et al exhibits less than 50% sequence identity with the probe to which the fragment hybridized. In the instant case, for example, the claimed nucleotide sequences would encompass a nucleotide acid with up to 5 kb mismatches across SEQ ID NO: 6. Without further guidance, undue experimentation would be required for a

person skilled in the art to generate and verify variants of SEQ ID NO: 1, 3, 5 and 6 and still have anti-Oomycetes activity.

6. Claims 1, 3-7, 39 and 44-46 remain rejected and claims 47-48 are rejected under 35 U.S.C. 1 12, first paragraph, because the specification, while being enabling for a method for increasing resistance of a plant to a plant pathogen of Oomycete by overexpression of a transgene encoding a Rpi-blb2 protein of SEQ ID NO: 2 or 4, does not reasonably provide enablement for nucleotide sequences encoding any Rpi-blb2 proteins, or any nucleotide sequences encoding any variant of SEQ ID NO: 2 or 4 as described in c)-d) of claim 1, or increasing activity of SEQ ID NO: 2 or 4 by others meanings including steps a)-e) of claim 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims, for the reasons of record stated in the Office action mailed January 8, 2008. Applicants traverse in the paper July 8, 2008. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that screening and testing for homologs or variants of Rpi-blb2 protein only require routine experiment and is not undue (response, page 17, 3rd paragraph). The examiner disagrees. As discussed above for written description rejection, the specification does not describe conserved structures of SEQ ID NO: 2 or 4 that are essential to its functional activity. Without correlating the conserved structure to the function, even if it is known in the art that conservative amino acid substitutions can

be made (the paragraph bridging pages 17-18), a person skilled in the art still would not know which residues can be modified and to which residue such substitution can be made. Therefore, without further guidance, to generate claimed genus of sequences is undue. For example, the sequence of SEQ ID NO: 2 consists of 1267 residues. A polypeptide having 82% identity to it differs in any over 220 residues. One skilled in the art would not just randomly change any 176 residues of SEQ ID NO: 2 or 4, by any type of addition, substitution, and/or deletion, to obtain a sequence that differs by 18%. One requires further guidance regarding the regions of SEQ ID NO: 2 or 4 that can tolerate change, and one requires guidance regarding the type of change that would be. The specification provides no guidance in that regard. Furthermore, Lazar et al. and Hill et al teach that making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results (previous office action, page 12, 2nd paragraph).

Finally, increasing the activity of Rpi-blb2 protein can be achieved in many ways including the meanings listed in steps a)-g) of claim6. However, the specification only teaches how to practice the invention by expressing anti-Oomycete protein of SEQ ID NO: 2 as a transgene in transgenic plant. The specification is silent as to how to use other methods to increase the activity of Rpi-blb2 protein. For example, the specification does not provide guidance on which genes are involved in up-regulating the expression of Rpi-blb2 protein (part (d) of claim 6), what exogenous inducing factors are (part (e) of claim 6), how to increasing specific activity/stability of the Rpi-blb2 protein (part (a) and (c) of claim 6), or how to stabilize the mRNA encoding resistance gene (part (b) of claim

6). Undue experimentation would be required to practice the invention using ways other than transgenically expressing Rpi-blb2 protein (previous office action, page 15, 1st paragraph). Applicants fail to respond the rejection in this regard.

Summary

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Li Zheng/

Examiner, Art Unit 1638